REMARKS

In an Office Action mailed May 4, 2005, the Examiner restricted Claims 1-69 into three groups. Applicants elected to prosecute the claims of Group III, with traverse of the subgroup restriction of Group III (e.g., pair-wise combination of cytoskeletal components), and with election of components of the microtubule system, ATPase assays and test compounds that can be classified as lead therapeutics for human disease as species for examination purposes. Applicants thank the Examiner for withdrawing the requirement for an election of a pair-wise combination of cytoskeletal elements. In the instant Office Action, the Examiner has withdrawn Claims 1-36 and 40-69 from consideration and raised the following rejections:

1) Claims 37-39 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement;
2) Claims 37-40 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite;
3) Claims 37-39 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,207,403 to Goldstein et al., priority date of January 8, 1998 (Goldstein);
4) Claims 37-39 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Sakowicz et al., Science, 280:292-295, April 10, 1998 (Sakowicz); and
5) Claims 37-39 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Stewart et al., Proc Natl Acad Sci USA, 90:5209-5213, 1993 (Stewart) and U.S. Patent No. 5,569,588 to Ashby et al., 1996 (Ashby).

Applicants hereby amend Claim 37, cancel Claims 1-36 and 38-69, and enter new Claims 70-73, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments. Applicants reserve the right to prosecute the original, similar, or broader claims in one or more future application(s). The amendments do not introduce new matter.

1) The Claims Meet the Written Description Requirement

The Examiner has rejected Claims 37-39 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner states:

> the specification does not disclose a representative number of species of the encompassed genera of all cytoskeletal systems and methods of identifying a therapeutic lead compound that modulates the activity of any cytoskeletal system, wherein detecting a change in coupling between ATP hydrolysis and force generation indicates that said compound modulates activity of a cytoskeletal system, so that the skilled artisan cannot envision the detailed component structures of any and all such cytoskeletal systems. ... The specification provides one example of such an assay procedure as per claim 37, wherein compounds from the marine sponge *Adocia sp.* inhibit the kinesin ATPase motor and its relationship to microtubules (Office Action, page 5).

Applicants respectfully disagree that the claims fail to comply with the written description requirement. Nonetheless, Applicants have amended Claim 37, canceled Claims 1-36 and 38-69, and entered new Claims 70-73, in order to further the prosecution of the present application and Applicant's business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants have amended Claim 37 to recite "wherein said cytoskeletal system is a microtubule system, and wherein said first component comprises a kinesin motor protein and said second component comprises a tubulin protein that specifically bind to each other." Support for this amendment is present in the application as filed, as noted by the Examiner. For instance support for these embodiments is found among the pairwise combinations of cytoskeletal components shown in Table 1, as well as in the exemplary embodiment described in Example 3. Likewise, new Claim 70 directed to methods "further comprising step iv) testing said test compound on a variety of ATPases," finds support in Example 3. For instance, Table 2 of Example 3 discloses the testing of a representative *Adocia* test compound on the activity of multiple enzymes including a plurality of ATPases. Lastly, new Claims 71-73, find support in the text of original Claims 25, 33 and 61, respectively.

As the new and amended claims meet the written description requirement, Applicants respectfully request that this rejection be withdrawn.

2) **The Claims Are Definite**

The Examiner has rejected Claims 37-40 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner has rejected Claim 37 alleging an uncertain antecedent basis for the terms "a cytoskeletal system" in lines 3, 4, and 9. Applicants

believe the claims as written are definite. Even so Applicants have amended Claim 37 to recite "said cytoskeletal system" in lines 3, 4 and 9, in order to further the prosecution of the present application and Applicant's business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). Accordingly, Applicants respectfully request that this rejection be withdrawn.

3 & 4) The Claims Are Novel

The Examiner has rejected Claims 37-39 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,207,403 to Goldstein et al., having a priority date of January 8, 1998 (Goldstein), and under 35 U.S.C. § 102(a) as allegedly being anticipated by Sakowicz et al., Science, 280:292-295, April 10, 1998 (Sakowicz). Applicants hereby correct the priority claim of the instant application by amending the Specification to recite that this "application is also a Continuation-in-Part of U.S. Application No. 09/724,609, filed on November 28, 2000, now U.S. Patent No. 6,489,134, which is a Divisional of U.S. Application No. 09/226,772, filed January 6, 1999, now U.S. Patent No. 6,207,403, which claims priority to U.S. Provisional Application No. 60/070,772, filed on January 8, 1998." Applicants note, that the instant application and the '609 application were *co-pending* during the period from January 16, 2002 (when the instant application was submitted to the US examining office with a petition for revival of the parent PCT application) to August 1, 2004 (when the '609 application issued as a patent). Applicants further note that Lawrence S. B. Goldstein is properly listed as an *inventor* of the instant application via a petition to correct inventorship received by the Office on August 15, 2005, as well as the applications of the '609 lineage. Moreover, the instant application is a nonprovisional application which entered the national stage after compliance with 35 U.S.C. 371 from an international application filed under 35 U.S.C. 363 before November 29, 2000 (e.g., *September 3, 1998*). As such, Applicants believe that the correction of the priority claim is proper in the absence of a surcharge and a petition to accept an unintentionally delayed priority claim. Thus the priority claim of the instant application now includes both the Goldstein patent (filed January 6, 1999) and the provisional application related thereto (filed January 8, 1998). As such, neither the Goldstein patent nor the Sakowicz publication pre-date

the invention by Applicants and therefore do not anticipate the pending claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

5) The Claims Are Not Obvious Over Stewart in View of Ashby

The Examiner has rejected Claims 37-39 under 35 U.S.C. § 103(a) as allegedly unpatentable over Stewart et al., Proc Natl Acad Sci USA, 90:5209-5213, 1993 (Stewart) and U.S. Patent No. 5,569,588 to Ashby et al., 1996 (Ashby). The Examiner states that Stewart teaches methods comprising providing a first component of a cytoskeletal system (e.g., kinesin or ncd) and a second component of a cytoskeletal system (microtubules) and

> detecting a change in coupling between ATP hydrolysis and force generation (see p. 5210, para 3-5, p.5212, Figures 1-2); wherein said change indicates that said compound modulates activity of a cytoskeletal system (p. 5213, para 2). Stewart et al. disclose the use of the drug taxol in preparing the microtubules (p. 5210).
>
> Stewart et al. does not disclose using the method of modulating the activity of a cytoskeletal system to identify a therapeutic lead compound.
>
> Ashby et al. ... teach that new compounds which interfere with tubulin-based cytoskeletal elements such as taxol, would provide candidates for taxol-like pharmaceuticals.
>
> It would have been prima facie obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used methods of modulating the activity of a cytoskeletal system, as taught by Stewart et al., to identify a therapeutic lead compound, as taught by Ashby et al. (Office Action, pages 10-11).

Applicants respectfully disagree that the claims are obvious over the Stewart / Ashby combination. A *prima facie* case of obviousness requires: some suggestion or motivation to combine the reference teachings; a reasonable expectation of success; and a teaching or suggestion of all claim limitations. Applicants submit that the Examiner did not meet all the requirements for establishing a *prima facie* case of obviousness.

In the first place, the Examiner contends that one of skill in the art would be motivated to combine the teachings of Ashby directed to reporter genes operably linked to transcriptional regulatory elements (see abstract and claims) with the teachings of Stewart directed to the use of truncated kinesin heavy chains and ncd proteins (see abstract) because:

> Ashby et al. teach that new compounds that interfere with tubulin-based cytoskeletal element, may provide candidate taxol-like pharmaceuticals; and because Stewart et al. teach assays for assessing modulation of the activity of

> kinesin or ncd gene product in a cytoskeletal system, and because Stewart uses taxol in preparing microtubules as a component in their assay (Office Action, page 11).

Applicants respectfully disagree with the Examiner's characterization of the teachings of Ashby and Stewart. In fact, the sole section of Ashby reciting the terms taxol or tubulin, teaches that since taxol has been shown to interfere with tubulin based cytoskeletal elements, that

> a dominant mutant form of tubulin provides a response profile informative for breast cancer therapies with similar modes of action to taxol. ... Thus any new compound that induces the same response profile as the dominant tubulin mutant would provide a candidate taxol-like pharmaceutical (Ashby, 1st paragraph of column 4).

In this context, Ashby clearly teaches the use of *mutant forms of tubulin* (not taught or suggested by Stewart) in assays of transcription, as opposed to the use of truncated forms of the *tubulin-binding motor proteins* in binding and ATPase assays of Stewart. As such, motivation to combine Ashby and Stewart has not been shown.

Additionally, Applicants refute the Examiner's statement that Stewart teaches "said change indicates that *said compound* modulates activity of a cytoskeletal system" (*emphasis added*). On the contrary, Stewart simply teaches that "the efficiency with which ATP hydrolysis is coupled to microtubule movement decreases drastically with increasing *truncation of KHC*" and that *ncd truncation* resulting in a "nearly 100-fold decline in motility rate is not accompanied by a 100-fold decline in enzymatic activity" (Stewart, page 5213, 1st and 3rd whole paragraphs, *emphasis added*). Applicants respectfully contend that detecting a change in coupling of ATP hydrolysis and force generation as a consequence of using a mutant second component of a cytoskeletal element does not provide the requisite expectation of success in detecting a change in coupling of ATP hydrolysis and force generation as a consequence of using a test compound. As there was no teaching or suggestion in the prior are cited by the Examiner that taxol would possess this combination of properties, a reasonable expectation of success in achieving the claimed invention is lacking in the Ashby / Stewart combination.

As the motivation to combine Ashby and Stewart is lacking, and even if combined a reasonable expectation of success is not present, Applicants contend that the claims are not obvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Conclusion

Applicants believe the amendments and arguments set forth above traverse the Examiner's rejections and therefore request that these grounds for rejection be withdrawed. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect before the mailing of a further Office Action.

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